quate justification,[7-10,12] depicted as having the same absolute stereochemistry as that of ilimaquinone (1). The hazards of such correlations are highlighted by a recent report[11] in which two compounds, structurally similar to ilimaquinone (1) but "enantiomeric" to it, were found to co-occur with ilimaquinone (1).

We have unambiguously established the absolute stereochemistry of ilimaquinone (1) by the following degradative approach and found it to be opposite to that previously proposed. Basic hydrogen peroxide oxidation of ilimaquinone[13] (1) followed by methylation with diazomethane yielded the ester 4. Acid-catalyzed rearrangement[14,15] of 4 gave the ester 5,[16] which possessed an optical activity ($[\alpha]_D$ -57.6° (*c* 0.25, $CHCl_3$)) comparable to that of the same compound obtained by degradation of aureol (6) (lit.[17,18] $[\alpha]_D$ -48.4° (*c* 0.4, $CHCl_3$)). The absolute stereochemistry of aureol (6) had previously been established[19] by X-ray analysis of a bromoacetate derivative. Thus the absolute stereochemistry of ilimaquinone (1) is the same as that of avarol (3).

Failure of the CD approach to predict the correct absolute stereochemistries in the 4-keto-5-methyl-*trans*-decalins described above highlights the need to exercise caution when attempting to assign absolute stereochemistries by interpreting weak CD effects.

**Registry No.** 1, 71678-03-0; 2, 109717-96-6; 3, 55303-98-5; 4, 109717-97-7; 5, 76215-39-9; 6, 72853-81-7.

(13) We are grateful to Prof. D. J. Faulkner for providing an authentic sample of ilimaquinone.

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(15) The possibility that acid-catalyzed isomerization might have induced epimerization or racemization about C8 was addressed by carrying out the reaction with deuteriated reagents (MeOD-DCl-AcOD). The C8 methine proton did not undergo exchange even under prolonged reaction conditions.

(16) The rearranged ester 5 was isolated as a stable colorless oil: $^1H$ NMR ($CDCl_3$) 0.84 (s, 3 H), 0.84 (d, 3 H, $J$ = 8.0 Hz), 0.95 (s, 3 H), 0.97 (s, 3 H), 3.66 (s, 3 H); $^{13}C$ NMR ($CDCl_3$) 16.2 (q), 19.9 (t), 20.8 (q), 25.3 (t), 25.7 (t), 27.1 (t), 27.6 (q), 29.3 (q), 29.4 (t), 30.8 (t), 33.8 (d), 34.5 (s), 39.9 (t), 40.4 (s), 51.6 (q), 131.6 (s), 138.0 (s), 175.1 ppm (s); EIMS $m/z$ 278 ($M^+$, 11%), 191 (100).

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(18) Preparation of the rearranged ester 5 by degradation of ambliol-B revealed[17] an $[\alpha]_D$ -52.9° (*c* 0.7, $CHCl_3$), which is in good agreement with that obtained from ilimaquinone (1).

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## A Novel Method for Regioselective 2′-O-Methylation and Its Application to the Synthesis of 2′-*O*-Methyl-5-[[(carboxymethyl)amino]methyl]-uridine

*Summary:* A new modified nucleoside, 5-[[(carboxymethyl)amino]methyl]-2′-*O*-methyluridine, was successfully synthesized by using a two-step O-methylation procedure involving alkylation of the 2′-hydroxyl group with 1,3-benzodithiolium tetrafluoroborate followed by Raney nickel reduction.

*Sir:* In recent years, much attention has been paid to the molecular mechanism of codon recognition by tRNA[1] since it has been proven that modified uridine derivatives located at the first position of anticodon played an important role in the regulation of rigidity/flexibility of the anticodon of tRNAs.[2] Quite recently, a 2′-O-methylated species (1) of 5-[[(carboxymethyl)amino]methyl]uridine (2) was discovered in the first letter of anticodon of *E. coli* $tRNA^{Leu}$.[3] It is of great interest to know how the 2′-O-methyl group affects the conformation of the sugar moiety. In this paper, we report a synthesis of 1 which involves a new procedure for the regioselective 2′-O-methylation.

Małkiewicz[4] reported the synthesis of 2 by an eight-step reaction from 2′,3′-*O*-isopropylideneuridine via 2′,3′-*O*-isopropylidene-5-(hydroxymethyl)uridine, which was easily obtained by the reaction of 3 with HCOH/KOH.[5,6] Reese[7] also synthesized 2 using displacement of the methiodide of 2′,3′-*O*-isopropylidene-5-(pyrrolidinomethyl)uridine with glycine *tert*-butyl ester. These facts led us to examine the 5-hydroxymethylation[5] and 5-(dialkylamino)methylation[8] of 2′-*O*-methyluridine (4) under similar conditions. However, several attempts to introduce these substituents at the 5-position of 4 have failed. These reactions required essentially the neighboring group participation of the 5′-hydroxyl group, as accounted for by Santi[9] and other workers.[10,11] Therefore, we searched for an alternative route to 2 in which the 2′-O-methylation was planned at a later stage. Reaction of 3 with 37% formalin–piperidine in 50% aqueous ethanol at 80 °C for 8 h gave quantitatively the Mannich base 5. This product was converted in situ to the methiodide 6 by treatment with 5 equiv of methyl iodide in DMF at room temperature for 20 min. The methiodide was allowed to react with 1 equiv of *N*-benzylglycine ethyl ester[12] in the presence of 1 equiv of $(i\text{-Pr})_2NEt$ at 60 °C for 4 h. This one-flask reaction gave finally 2′,3′-*O*-isopropylidene-5-[[*N*-benzyl[(ethoxycarbonyl)methyl]amino]methyl]uridine (7) in an overall yield of 64%. The deacetonization of 7 by the use of 20% acetic acid at 90 °C for 3 h resulted in the triol 8 in 52% yield. Since 8 was unstable under both acidic and basic conditions, the 2′-O-methylation should be done under neutral conditions.

Several methods are known for the 2′-O-methylation of uridine.[13] Moffatt[13b] reported that treatment of 2′,3′-

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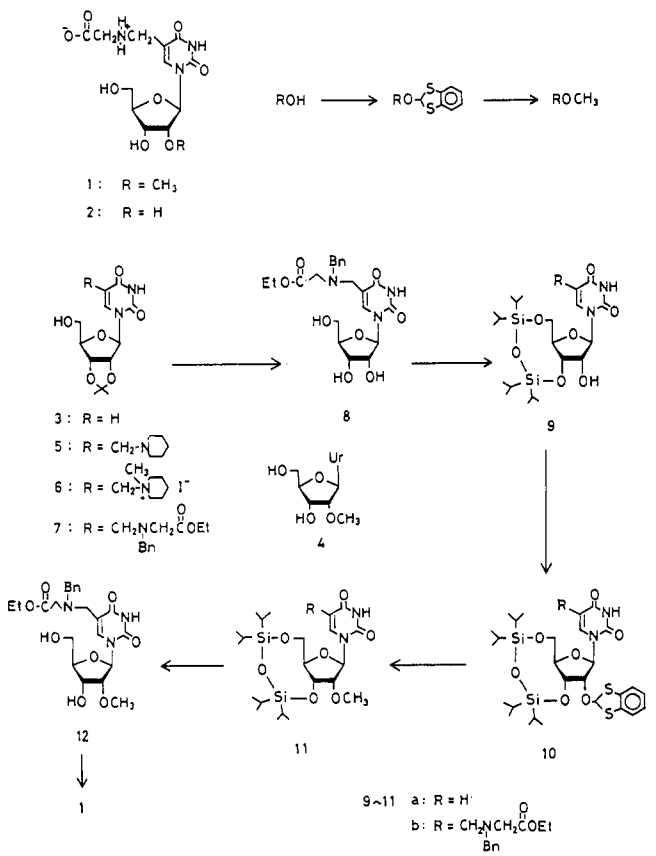
(12) Małkiewicz[4] has already reported the use of the N-benzyl group for protection of the secondary amine, since without protection of the amino function decomposition occurred during chromatography. The benzyl group is also used for avoidance of N-alkylation at the branched chain in the conversion of 9 to 10.

0022-3263/87/1952-5060$01.50/0 

**Scheme I**



*O*-(dibutylstannylene)uridine with methyl iodide gave a 55:45 mixture of the 2′- and 3′-methylated species. Tin(II) chloride catalyzed methylation of uridine by use of diazomethane resulted in a mixture of 2′- and 3′-O-methyl isomers which were isolated in 58% and 28% yields, respectively, by tedious chromatographic separation.[13c] Methylation of 5′-O-trityluridine with diazomethane afforded a better selectivity but still required careful sepration from the 3′-isomer and acidic treatment for removal of the trityl group.[13d] Recently, we[13e] and Chattopadhyaya[13f] reported the 2′-O-methylation of $N^3$-protected 2′,3′-(tetraisopropyldisiloxane-1,3-diyl)uridine derivatives with MeI/$Ag_2O$. Although these procedures accomplish the regioselective 2′-O-methylation, they require protection of the imido group of the uracil moiety and ultimately could not be applied to **8** because of the simultaneous methylation on the tertiary amine residue. These problems led us to study an alternative methylation procedure for **8**. Finally, we found a new method for the 2′-O-methylation as shown in the Scheme I.

The present method involves a two-step reaction. First, the alcoholic function is protected with the 1,3-benzodithiol-2-yl (BDT) group as previously reported by us.[14] The protected species is then treated with Raney Ni (W-2) in refluxing ethanol. For example, treatment of 2′-*O*-(1,3-benzodithiol-2-yl)-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)uridine (**10a**)[15] with Raney Ni in ethanol under reflux for 1.5 h gave the 2′-*O*-methyluridine derivative (**11a**) in 58% yield, which was converted to **4a** in 78% yield by treatment with KF–$Et_4NBr$/$CH_3CH$–$H_2O$. Application of this procedure to the synthesis of **1** was performed as follows: The reaction of **8** with Markiewicz reagent[16] gave a 3′,5′-cyclic silyl ether derivative (**9b**) in 93% yield. Compound **9b** was treated with Nakayama reagent (1,3-benzodithiolium tetrafluoroborate)[17] in the presence of pyridine in methylene chloride at room temperature for 2.5 h gave the 3′-protected product (**10b**) in 70% yield. The Raney Ni reduction of the 2′-O-BDT ortho ester gave the 2′-O-methyl derivative (**11b**) in 51% yield. Desilylation of **11b** afforded **4b** in 88% yield. The catalytic hydrogenation of **4b** on Pd/C gave **12** in 33% yield. Finally, the hydrolysis of **12** by dilute NaOH followed by neutralization and then paper chromatography on Whatman 3MM using *i*-PrOH–concentrated $NH_3$–$H_2O$ (7:1:2, v/v/v) gave **1** in 42% yield. The product **1** was identified with the authentic material from $tRNA^{Leu}$ by comparison with the 400-MHz NMR spectrum.

**Registry No.** **1**, 110419-13-1; **3**, 362-43-6; **4**, 2140-76-3; **4b**, 110419-11-9; **5**, 110419-05-1; **6**, 110419-06-2; **7**, 110419-07-3; **8**, 110419-08-4; **9b**, 110419-09-5; **10b**, 110433-14-2; **11b**, 110419-10-8; **12**, 110419-12-0; Bn-Gly-OEt, 6436-90-4; 1,3-benzodithiolium tetrafluoroborate, 57842-27-0.

**Supplementary Material Available:** Full NMR spectral data for new compounds **1** and **7**–**12** (2 pages). Ordering information is given on any current masthead page.

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*Received May 20, 1987*

## The First Versatile and Practical Building Blocks Equivalent to the Synthon of Monofluoromethylene Dicarbanion

*Summary:* New monofluorinated synthons have been prepared. The use of α-fluoro-α-nitro carboxylic esters as versatile building blocks was demonstrated by their conversion to various monofluorinated compounds via fluoromethyl anion and fluoromethylene dianion equivalents.

*Sir:* Fluorine-containing organic compounds have recently received increasing interest from both a new material[1] and a biological activity[2] viewpoint. However, the methods for

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